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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,925	05/30/2001	Richard J. Feldmann	3124-Z	5146

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EXAMINER	
BRUSCA, JOHN S	

ART UNIT	PAPER NUMBER
1631	

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09/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/866,925	FELDMANN, RICHARD J.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action contains new grounds of rejection under 35 U.S.C. 101 for non-statutory subject matter and 35 U.S.C. 112, first paragraph for new matter not necessitated by the applicant's amendment filed 19 July 2007 and is therefore a non-final action.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 20-37 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 20-37 are drawn to a process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). The instant claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be "tangible," the process must

produce a real world result . Furthermore, the claim must be limited only to statutory embodiments.

Claims 20-37 do not require production of a tangible result in a form that is useful to the user of the process or apparatus. The claims conclude with a step of outputting the results to a utilization facility. The final step does not require that the output of the method is in a format that can be understood by a user. A tangible result requires that the claim as a whole must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 26 is rejected under 35 U.S.C. 102(b) as being anticipated by Fleischmann et al.

The claim is drawn to a method of sequencing a genome, determining transcriptional control regions, and outputting the results.

Fleischmann et al. shows in the abstract and throughout a method of sequencing the genome of Haemophilus influenzae. Fleischmann et al. shows in Table 1 a step of annotation of

the genomic sequence that includes regulatory regions. Fleischmann et al. shows on pages 508-509 that the data was deposited in a publicly accessible database facility, the Genome Sequence DataBase.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 20-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method which concludes with a step of outputting a result to a utilization facility. The specification at the time of filing does not describe outputting a result to a utilization facility.

7. Claims 20-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a

determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) Quantity of experimentation: The only utility asserted by the specification is to use connectron symmetries to predict control of gene expression (see for example pages 10, 11, 14, and 15 of the specification).In order to practice the claimed invention one of skill in the art must identify and use a connectron to predict regulation of gene expression. In some embodiments changes in connectron behavior that correlate with changes in gene expression is monitored or effected. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The amount of direction or guidance presented: The claimed invention is a method of identification of sequences that have a connectron relationship and act to modulate gene expression. On page one, the specification defines connectrons as a tetradic structure between two sequences in an RNA transcript of a genomic sequence and two sequences in double stranded genomic DNA. Figure 4 depicts a connectron. The specification speculates without evidence on pages 1-3 that triple-stranded (triplex) structures will form between RNA and double stranded DNA in chromatin where connectron symmetries are identified. The specification does not provide guidance that there are any limitations on formation of triplex structures, and only implies that regions of RNA with identical sequence to one strand of a

double stranded DNA sequence will form triplex structures. The specification does not address why all RNA transcripts of genes would not form a continuous triplex structure with the gene from which it is transcribed. The specification provides guidance to identify connectron symmetries in genomic sequences on pages 31-34. The specification does not provide detailed guidance to use identified connectron symmetries because the specification does not show whether or not connectrons as depicted in figure 4 form within cells or have an effect on gene expression. The specification does not provide specific guidance for monitoring or effecting changes in connectron behavior that correlate with gene expression.

c) The presence or absence of working examples: The specification provides working examples of identification of connectron symmetries by computer-mediated searching of genomic sequences in pages 35-188. However, the specification does not provide evidence that connectron symmetries in genomic sequences result in formation of triplex RNA-DNA structures or that if connectron triplex structures do exist that connectrons control gene expression. The specification does not provide working examples of using identified connectron symmetries to predict effects on gene expression. The specification does not provide working examples of monitoring or effecting changes in connectron behavior that correlate with gene expression.

d) The nature of the invention: The nature of the invention, gene expression control, is complex.

e) The state of the prior art: One of skill in the art, after reading the specification, would not know that connectron symmetries identified by computer-mediated searches of genomic sequences would allow for prediction of gene expression of genes that have connectron

symmetries. The specification does not provide experimental evidence that connectron symmetries cause modulation of gene expression. Neither the prior art nor post-filing art shows connectrons. Mattick (published in 2001, one year after the effective instant filing date) reviews effects of RNA molecules on gene regulation. Mattick does not show connectrons as defined in the instant specification. Chan et al. reviews triplex DNA formation. Chan et al. shows in figures 1A-C that short stretches of oligonucleotides may form parallel or antiparallel triplex structures. Chan et al. shows in figures 1B that parallel triplex forming oligonucleotides form bonds between C and T residues of the oligonucleotide and G and A residues of the double stranded DNA molecule. Figure 1C shows that antiparallel triplex forming oligonucleotides form bonds between A, G, and T residues of the oligonucleotide and A, G, and A residues of the double stranded DNA. Chan et al. characterize the limited range of base pairing possibilities in triplex structures as pyrimidine binding motifs or purine binding motifs. Chan et al. describe on pages 268-273 the unpredictability and difficulty of forming desired triplex structures that are limited to the purine motif or the pyrimidine motif. Chan et al. does not show a mechanism that allows for triplex structures to form with any and all regions of identity between an RNA transcript and a region of double stranded DNA that has an identical sequence in one of the two strands of DNA, as required for connectron formation as defined in the instant specification.

f) The relative skill of those in the art: The skill of those in the art of gene expression is high.

g) The predictability of the art: The predictability of the relationship of connectron symmetries and gene expression is unknown in the prior art and is not described in the instant

specification.

h) The breadth of the claims: The claims are broad in that they are drawn to identification and modulation of connectron symmetries whose relationship to gene expression is not established.

The skilled practitioner would first turn to the instant specification for guidance in using the claimed invention. However, the specification lacks any evidence that connectrons form in cells or that connectron symmetries are related to gene expression. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss connectron symmetries. Chan et al. shows that triplex formation occurs only with oligonucleotides with a purine rich or pyrimidine rich motif, rather than with any identical sequence as suggested in the specification. Finally, said practitioner would turn to trial and error experimentation to determine a relationship between connectron symmetries and gene expression. Such amounts to undue experimentation.

8. The rejection of claims 20 and 28-37 as indefinite under 35 U.S.C. 112, second paragraph in the Office action mailed 24 January 2007 for recitation of the term "data" in lines 4, 7, 8, 13, and 14 because it is not clear how sequence data can bind RNA molecules as recited in claim 20 is withdrawn in view of the amendment filed 19 July 2007.

9. The rejection of claim 28 as indefinite under 35 U.S.C. 112, second paragraph in the Office action mailed 24 January 2007 because it is not clear if the C1 and C2 sequences are genomic sequences that are transcribed and appear as adjacent sequences in the RNA molecule is withdrawn in view of the amendment filed 19 July 2007.

10. The rejection of claim 20 as indefinite under 35 U.S.C. 112, second paragraph in the Office action mailed 24 January 2007 because it is not clear if there is a gap between the T1 and T2 sequences is withdrawn in view of the amendment filed 19 July 2007..

11. On further consideration the rejection of claim 24 as indefinite under 35 U.S.C. 112, second paragraph in the Office action mailed 24 January 2007 because it appears to require a physical step is withdrawn.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 20-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is indefinite because it is not clear if the method requires identification of single stranded DNA sequences or double stranded DNA sequences that bind RNA sequences, i.e., it is not clear if the method identifies connectrons that comprise triple helical regions as defined in the specification on pages 6-7.

Claim 20 and 29-37 are indefinite because it is not clear if the C1 and C2 sequences are genomic sequences that are transcribed and appear as adjacent sequences in the RNA molecule, that is it is not clear that the C1 and C2 sequences form a C1/C2 sequence as defined in the specification at page 6.

Claims 21-25 and 27 are indefinite because the claims appear to require steps of physical transformations to cells comprising the genomic sequences analyzed by the claimed methods, but

the claim states that the methods are computer mediated. Claims 21 and 22 have limitations that changes in connectron behavior are detected which suggests the claimed method requires physical manipulation of cells to cause a change that is detected. Claim 23 requires comparison of preexisting behavior and behavior of a newly introduced gene which suggests that the method requires physical manipulation of cells to introduce a gene. Claim 25 requires measuring the effect of changing expression of different gene collections which suggests that the method requires physical manipulation of cells. Claim 27 requires measuring a response of a cell to a change in the environment or genetic composition which suggests that the method requires physical manipulation of cells.

Claim 26 is indefinite for recitation of the phrase "sites of target application" because the meaning of the phrase is not clear.

Response to Arguments

14. Applicant's arguments filed 19 July 2007 have been fully considered but they are not persuasive.

The applicant's state that Fleischmann et al. does not show all of the limitations of claim 26. The quotation of claim 26 in the applicant's arguments includes items in parentheses that are not in the pending claim. The preamble to claim 26 is merely an intended use that does not serve as antecedent basis for any claim term, and is therefore not given patentable weight. No other term or phrase of claim 26 limits the claimed subject matter to detection of connectrons as defined in the specification. Fleischmann et al. performs all of the claimed steps. The applicants state that Fleischmann et al. does not determine sites of control sequences but Fleischmann et al.

determines sites of promoters which are control sequences. The applicants state Fleischmann et al. does not determine a target application site, however the limitation is in the alternative and is not a required embodiment of the claimed subject matter.

The applicants state that the issues discussed in the rejection for lack of enablement under 35 U.S.C. 112, first paragraph are unrelated to the claimed subject matter, however enablement requires that one of skill in the art is enabled to use the claimed subject matter, and the rejection is maintained because the specification at the time of filing does not enable the use of the claimed subject matter. The Board noted in the Vacatur mailed 28 September 2006 that one of skill in the art would be enabled to generate data of connectron symmetries from a genome sequence. However, the applicants have not provided any evidence in the specification or their arguments that the triplex structure of connectrons form or can be used to predict or control gene expression. The applicants argue that the claim limitations do not require that the results of the claimed methods be used to predict or control gene expression, but enablement of the claimed subject matter does require that there is an enabled patentable utility for the claimed subject matter. For this reason the rejection is maintained because a use for the claimed subject matter is not enabled.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/John S. Brusca/

Primary Examiner

Art Unit 1631

jsb